Original article

Early life stress explains reduced positive memory biases in remitted depression

J.A. Gethin a, K.E. Lythe a, C.I. Workman a, A. Mayes a, J. Moll b, R. Zahn a,c,*

a Division of Neuroscience and Experimental Psychology, The University of Manchester, Manchester M13 9PL, UK
b Cognitive and Behavioral Neuroscience Unit, D‘Or Institute for Research and Education (IDOR), 22280-080 Rio de Janeiro, RJ, Brazil
c Institute of Psychiatry, Psychology & Neuroscience, Department of Psychological Medicine, Centre for Affective Disorders, King’s College London, London SE5 8AZ, UK

ABSTRACT

Background: There is contradictory evidence regarding negative memory biases in major depressive disorder (MDD) and whether these persist into remission, which would suggest their role as vulnerability traits rather than correlates of mood state. Early life stress (ELS), common in patients with psychiatric disorders, has independently been associated with memory biases, and confounds MDD versus control group comparisons. Furthermore, in most studies negative biases could have resulted from executive impairments rather than memory difficulties per se.

Methods: To investigate whether memory biases are relevant to MDD vulnerability and how they are influenced by ELS, we developed an associative recognition memory task for temporospatial contexts of social actions with low executive demands, which were matched across conditions (self-blame, other-blame, self-praise, other-praise). We included fifty-three medication-free remitted MDD (25 with ELS, 28 without) and 24 healthy control (HC) participants without ELS.

Results: Only MDD patients with ELS showed a reduced bias (accuracy/speed ratio) towards memory for positive vs. negative materials when compared with MDD without ELS and with HC participants; attenuated positive biases correlated with number of past major depressive episodes, but not current symptoms. There were no biases towards self-blaming or self-praising memories.

Conclusions: This demonstrates that reduced positive biases in associative memory were specific to MDD patients with ELS rather than a general feature of MDD, and were associated with lifetime recurrence risk which may reflect a scarring effect. If replicated, our results would call for stratifying MDD patients by history of ELS when assessing and treating emotional memories.

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1. Introduction

Patients with current major depressive disorder (MDD) have demonstrated biases towards better recall of negative than positive materials [1–3]. This is consistent with Bower’s associative network theory of memory and emotion [4], which profoundly influenced the cognitive psychology of depression by proposing a close link between mood states, emotions, and memory. Despite nearly 40 years of researching this hypothesis, key questions remain. Two particularly relevant questions are whether emotional biases in memory can act as vulnerability factors outside of depressive episodes and whether they are specific for MDD.

The bias of better memory for negative compared to positive materials in MDD has been demonstrated most clearly with non-autobiographical stimuli and active recall tasks [5]. Using the Autobiographical Memory Test, however, impaired retrieval of contextual details for positive relative to negative events was only found in some studies in current [6] and remitted MDD (rMDD) [8,9]. A valence-independent impairment, however, was the most robust finding in a meta-analysis [10] and in the largest study in rMDD to date [11]. Despite inconsistencies about valence-effects, impaired autobiographical memory persisted into remission [8,9,11] suggesting its possible role in vulnerability [12]. Abnormalities on the Autobiographical Memory Test, however, are best accounted for on the basis of executive dysfunction [13,14] rather than contextual memory per se, and performance is influenced by retrieval strategy [15].

Passive memory tasks avoid confounding patients’ performance with executive impairments, which could result simply from being
distracted by depressive thoughts [16], although this literature is much sparser and more inconsistent. When priming is used to probe memory for semantically encoded materials, people with current MDD/dysthymia favoue negative over positive materials, which is the opposite of healthy control participants [17]. In contrast, studies using a recognition memory task demonstrated intact recognition memory for both positive and negative materials [18–20] despite impaired valence-independent recall [19] in current MDD or, intriguingly, decreased negative and intact positive recognition memory in pregnant women with rMDD [21]. One study found subtle effects of personal relevance rather than valence or overall recognition memory performance in current MDD [20]. We found only one study demonstrating impaired emotional recognition memory in MDD, which was conducted in a symptomatic group and found no valence effect on accuracy [22]. One explanation for the heterogeneity in the passive memory literature that has not yet been investigated is that memory biases in MDD are due to the exposure of many patients to early life stress (ELS, [23]), which is usually absent in the typical healthy control population.

ELS itself was associated both with impaired retrieval of contextual details of emotional memories [24–26] and with a reduced positive memory bias [27]. Furthermore, ELS has been linked to stress hormone [30] and mediate established emotional memories in animals and humans [28]. The same medial temporal lobe structures have been demonstrated to underpin associative memory for temporal and spatial contexts in humans [29]. Some studies, however, report no consistent link between ELS and impaired emotional memory using the autobiographical memory test [30,31] and a review suggested that experiencing depressive or post-traumatic reactions to stressors is necessary for impaired emotional memory, rather than stressful events or a history of ELS alone [32]. It is thus unclear whether MDD itself is associated with emotional memory biases, or whether this effect is mediated by ELS. This is because ELS has not been controlled for in the literature using more specific tests of contextual memory (i.e. passive memory tests) rather than those, which are confounded by executive functioning (e.g. Autobiographical Memory Test).

Given the close link between memories and mood postulated by Bower [4], one could postulate that the reduced positive memory biases sometimes reported in MDD contribute to the reductions in positive affect predicted to be specific to MDD by the decreased positive emotionality model of MDD [33]. In contrast, blame attribution models of MDD [34,35] would predict that MDD vulnerability is related to selective overgeneralisation of self-blame-related memories, due to lack of access to contextual details, relative to blaming others (other-blame). This prediction would be made under the hypothesis that blame biases may be influenced by memory biases and vice versa. Corroborating evidence for a self-blaming emotional bias as a vulnerability factor for MDD was recently provided by showing reduced other-blaming relative to self-blaming emotions in rMDD [36,37]. To our knowledge, self-blame-related memory biases have not been investigated in MDD, and the literature on the importance of self-reference effects when encoding emotional materials in mediating emotional memory biases in MDD is inconsistent [5,17,38].

In order to prove associative memory for temporal and spatial contexts of emotional materials per se, rather than the process of retrieving such information as probed on tasks, such as the Autobiographical Memory Test, we used a simple recognition memory task, which largely avoids the confounding effects of executive functions [39,40]. This novel task was free of autobiographical components to allow strict experimental control of the relevant variables and is therefore only comparable with the Autobiographical Memory Test in that both require the spatio-temporal encoding and recognition of emotional information; otherwise these tests bear no resemblance. We designed this novel test through manipulation of temporal and spatial contextual details in statements describing social actions, derived from norms, which provided participants with positive and negative emotionally relevant concepts. This task was balanced across conditions to allow separate investigations of both valence- and blame-related biases. We investigated whether vulnerability to MDD rather than its symptoms is associated with emotional memory biases by studying a medication-free group of patients in full remission from symptoms [41], known to be at high lifetime risk of MDD [42], and compared against a healthy control group with no personal or family history of MDD. We probed whether MDD itself or only its interaction with ELS would be associated with emotional memory biases by comparing rMDD patients with and without a history of ELS.

We tested the alternative predictions of the self-blaming bias and positive emotionality models of vulnerability to MDD on associative memory for temporal and situational context. We favoured the hypothesis that rMDD patients would show self-blame-selective rather than negative or positive emotion-selective changes in associative memory compared to a healthy control (HC) group. We also hypothesised that this self-blaming bias would be stronger in patients with ELS. These hypotheses were based on our previous finding of an overall increase in proneness towards experimentally induced self-blame-related emotions (self-disgust/contempt) relative to blaming others (disgust/contempt towards others) in rMDD with no overall change in positive or negative emotional biases [36]. Given the proposed importance of the medial temporal lobe memory system in MDD [43] and its guilt-selective functional disconnection from the conceptual-semantic representations of social behaviour in the right anterior temporal lobe [44], we hypothesised that self-blaming emotional biases could arise in part by biasing associative memory mechanisms shown to be hosted by the medial temporal lobe [29].

2. Methods

2.1. Participants

Potential participants responded to print and online advertisements (see Table 1) for the UK Medical Research Council-funded project “Development of Cognitive and Imaging Biomarkers Predicting Risk of Self-Blaming Bias and Recurrence in Major Depression”. Suitable participants gave written informed consent and were assessed by a senior psychiatrist (RZ) and with the Structured Clinical Interview–for DSM–IV–TR [45]. All participants were right handed as they also underwent neuroimaging. For inclusion in the rMDD group, participants had at least one previous MDE lasting at least two months, had been in remission for at least six months, and were free from centrally active medications (except hormonal contraceptives). They also had no current co-morbid or relevant past axis-I disorders to ensure group differences were due to vulnerability to MDD specifically rather than to the effects of other conditions. For the HC group, participants had no personal/first-degree family history of MDD. For full details of inclusion/exclusion criteria and recruitment procedures, see [36]. Participants were reimbursed for their time and travel costs. This research study was approved by the South Manchester NHS Research Ethics Committee (07/H1003/194).

In total, 707 participants gave oral consent to an initial telephone screening interview. Reasons for excluding participants are detailed in Table 1. Fifty-five rMDD and 30 HC participants completed the associative memory for social actions task. Data were excluded for two MDD participants due to current depression at the time of task completion and for six HC participants due to definite or questionable ELS. This paper reports a three-group
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